REMARKS

Entry of the foregoing and reexamination and reconsideration of the subject application, as amended, pursuant to and consistent with 37 C.F.R. § 1.112, are respectfully requested in light of the remarks which follow.

Claims 1-21, 23-31, 33-46, 48-86, 88-89, 101-108 and 110-137 are pending. Claims 2-21, 26-31, 33-46, 48-86, 88-99, 101-108, 110-125 and 127-137 stand withdrawn. Applicants note with appreciation the Office Communication of September 30, 2003, correcting the claims marked as withdrawn on the Office Action Summary page in the outstanding Office Action.

Claims 1, 24-25, and 76 are amended herein to address informalities such as spelling errors and grammar. Thus, no new matter is submitted by way of this Amendment.

Priority Documents

Certified copies of Swedish Application Nos. 9801164-6 and 9900319-6 are submitted herewith.

Objections to the Specification

The specification has been amended to claim benefit to International Application No. PCT/SE99/0054, filed on March 31, 1999, and Swedish Application Nos. 9801164-6 and 9900319-6.

Objection to the claims

Claims 2, 24-25 and 76 stand objected to for purportedly being inconsistant in the recitation of "No." and "no." as well as reciting an improper spelling of "homologs". Applicants assume that claim 1 is objected to, rather than claim 2, as claim 2 stands withdrawn. Claims 1 and 24-25 are amended herein to address these issues. With regard to claim 76, the Office Action does not state as to why claim 76 is objected to, and Applicants note that this claim does not depend on any other claim, nor does it recite a sequence identifier "No." or "homologue". Thus, the objections are obviated.

Objection under 35 U.S.C. § 132

The Office Action asserts that the recitation of "N" as inosine in the sequence listing filed on June 19, 2002 is new matter. Applicants submit that this is not new matter. It is well accepted that the computer software used in preparation of sequence listings will not accept "I" as inosine. Thus, "N" is the accepted code for the amino acid inosine in sequence listings before the U.S. Patent and Trademark Office. Applicants note with appreciation the attention of Mark Spencer and SPE Christopher Low in this regard.

Rejections under 35 U.S.C. § 112, Second Paragraph

Claims 1, 24-25, 76 and 126 stand rejected under 35 U.S.C. § 112, second paragraph, as purportedly indefinite.

Claim 76 stands rejected for the recitation of the phrase "fragment of said integrin". The Examiner argues that an article such as "a" should be inserted in front of the phrase. Claim 76 is amended herein to recite "a".

Claims 24 and 25 stand rejected for the recitation of the phrase "from about amino acid No", as it is purportedly unclear how many amino acids constitute "about". Applicants submit that the meaning of "about" as recited in claims 24-25 would be clear to the skilled artisan, as this word is commonly recited in similar context in many issued patents and is well-accepted.

Claim 1 stands rejected for the recitation of "same biological activities". Applicants submit that the specification provides the skilled artisan with the definition of "same biological activities". Specifically, the specification provides discussion as to the specific biological activities of the integrin subunit α10, and the sequences comprising same. Page 7 of the specification recites specific biological activities such as binding to markers, targeting of cells or tissues expressing the integrin subunit α10. Page 10 of the specification discusses binding entitites which bind the integrin subunit α10, as well as homologs or fragments thereof. Thus, the skilled artisan would be clearly apprised as to what is meant by "same biological activites".

Rejections under 35 U.S.C. § 112, First Paragraph

Claims 1, 23-25, 76 and 126 stand rejected under 35 U.S.C. § 112, first paragraph, as purportedly containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to make and/or use the invention.

The Office Action states that besides the collagen binding integrin subunit α10 comprising the amino acid of SEQ ID NO: 2 or fragment of SEQ ID NO: 10, wherein fragment is SEQ ID NO:7, amino acid 952-986 of SEQ ID NO:2, or amino acid 140-337 of SEQ ID NO: 2, the specification does not provide a sufficient enabling description of the claimed invention. The Office Action states that the skilled artisan would not know which sequences are essential, which sequences are non-essential, and what particular sequence lengths identify essential sequences. Applicants traverse.

The Office Action states that undue experimentation is required to determine the specific homologs, fragments and heterodimers of the α10 subunit; and which specific amino acid sequences are essential and which amino acid residues are most tolerant to modification and which must be conserved.

The factors to be considered in determining whether undue experimentation is required include the quantity of experimentation necessary, the amount of direction or guidance presented, and the presence or absence of working examples, the nature of the invention, the state of the prior art, the relative skill of those in the art, the predictability or unpredictability of the art and the breadth of the claims. In this regard, Applicants provide

the following comments to show that undue experimentation is not required and that the claims are enabled.

Fragments and Homologues

With regard to fragments, Applicants submit undue experimentation would not be required to determine appropriate fragments. Applicants note that the specific fragments of α10, as known at the date of filing, are defined in the specification as the I-domain, the splice domain, the cytoplasmic domain and the transmembrane domain, including the I-domain, the splice domain, the cytoplasmic domain and the transmembrane domain. Specific fragments of the heterodimer include the α10 subunit or the β subunit.

Applicants submit undue experimentation would not be required to determine appropriate homologues. Homologues are defined in the application as "essentially the same molecules from other species". This definition is also provided to the skilled artisan in the *Oxford Dictionary of Biochemistry and Molecular Biology* (attached hereto), as defined as "of proteins from different species having identical or similar functions". Furthermore, it is well known in the art that different integrins and subunits thereof are not homologues to each other. In fact, integrin α subunits are different proteins with different properties and functions. Thus, they are not interchangeable with each other. Integrin α subunits share an overall identify of only 20-40% (*see* the specification, page 15, lines 23-24). In addition, the α units are located on different chromosomes.

It is also well known entities exist, from different species, that are functionally equivalent, even if there are differences in the respective amino acid sequences. These entities are referred to as homologues, and in the present invention, these entities are the integrin α10 subunits. Because other integrin α subunits are not functionally equivalent, and thus not interchangeable, they are not homologues to the integrin α10 subunit.

In light of the above remarks, Applicants submit that human integrin α10 is not a homologue to, for example, human integrin α1-9. Instead, integrin α10 has homologues in other species, such as bovine or murine α10. Furthermore, because the sequence for human α10, and its fragment as defined above are disclosed in the present specification, Applicants submit that undue experimentation would not be required for the skilled artisan to practice the present invention. Undue experimentation would not be required for the skilled artisan to locate appropriate fragments or homologues because these techniques (such as hybridization techniques, RT-PCT techniques, immunoprecipitation and immunoblots) are well known in the art. Using what is provided in the specification with these well known techniques would only require basic experimentation on the part of the skilled artisan, rather than undue experimentation.

Furthermore, both sequences and detailed protocols are given in the present specification describing how to identify and isolate human α10 and said fragments (the I-domain, the splice domain, the cytoplasmic domain and the transmembrane domain). In fact, results of the identification and isolation experiments are provided in the specification.

Thus, Applicants submit that both fragments, as identified above, and homologues of integrin α10 would be easily identified and isolated by the skilled artisan for the skilled artisan without undue experimentation.

Heterodimers

Regarding heterodimers, Applicants note that isolated α- or β-subunits do not appear on cell surfaces. It is well known in the art that integrin heterodimers are assembled intracellularly and transported to the plasma membrane after synthesis. The β1-subunit is synthesized in excess of the α subunits, and resides in a large pool assuring a constant supply of subunits that can associate with newly synthesized α-subunits. The regulation of integrin synthesis appear to be exerted at the level of α-subunits in the systems studied. Thus, increases in integrin expression are achieved via increases in the synthesis of particular α-subunits.

This is particularly important to expression via transfection of integrin heterodimers. The cells that are transfected with the integrin α10 already contain sufficient amounts of the corresponding β1 subunit to form the α10 β1 heterodimer. Expression of recombinant proteins is a well-known technique to the skilled artisan. The method of transfection of α10 involves the use of the GenePORTER transfection reagent, which is based upon the procedure of lipofection. Transfection of integrins into cells is a well-known technique. Specific to the present invention are the transfection of α2β1 into HOS cells.

Regarding information as to which specific amino acid sequences are essential, which amino acid residues are most tolerant to modification and which must be conserved, Applicants submit that the skilled artisan would be able to locate recognizable domains of the integrins within each of the four collagen binding integrins using sequence alignments α10, α1, and α2 (*see* Appendix A, showing sequence alignment of four collagen binding integrins α10, α11, α1 and α2). The deduced amino acid sequences from α1, α2, α10, and α11 have been compared and it was found that those recognizable domains that are conserved between the four integrins. Even before the present application was filed, sequence alignments of α10, α1 and α2 were easily performed by the skilled artisan without undue experimentation. Thus, Applicants submit it would be clear to the skilled artisan as to which specific amino acids sequences are essential, which amino acid residues are most tolerant to modification and which must be conserved.

By way of explanation, Applicants provide the following comments about the I-domain, the cytoplasmic domain and the splice domain.

I-domain

The I-domain of the α10 integrin is 69% identical to the I-domain of α11 and the transmembrane domain is 87% identical to α11. If the skilled artisan were to look at a sequence within the I-domain and "BLAST" the sequence, a person skilled in the art would be able to identify it as an integrin (because there are only 4 collagen-binding, I-domain integrins.

The sequence VIVLDGSNSIYPW encompassing residues 147-159 at the N-terminus of the I-domain is completely conserved among α10, α11 and α1 subunits. In contrast, the cytoplasmic domains of α10, α11, α1 and α2 are all very different, except for a conserved GFF motif. GFF is believed to act as a hinge keeping the integrin in an inactive conformation. The ligand-binding specificity of the collagen-binding integrins also varies. In the α2 I-domain, D^{219} is important for binding to collagen type I. Mutating D to R at this position abolishes the ability of α2 to adhere to collagen type I. In the α I-domain, which displays a higher affinity for collagen type IV, the corresponding amino acid is R^{218}. In the α10 and α11 these positions are filled by $R2^{41}$ and T^{238}, respectively.

Cytoplasmic Domain

Applicants note that α10 is unusual in that the membrane proximal region of the cytoplasmic domain contains a GFFAH sequence instead of the integrin α consensus motif GFF(R/K)R. This motif is conserved throughout the integrin family and would therefore be clear to the skilled artisan that this identified an integrin.

Splice Domain

The α10 chain is an I-domain collagen-binding integrin which may be subject to alternative splicing. In the human, a region corresponding to exon 25 is spliced in or out.

Seq ID No 2 as a marker

Applicants refer the Examiner to Appendix B for information regarding the use of the subunit recited in SEQ ID NO:2 as a marker in transplants. The results of the FACS analysis show that primary human chondrocytes may be identified by use of a mAb against α10. Collagen type II and aggrecan in the cells are further measured by quantitative PCR, both which are known markers of chondrocytes and are routinely measured by mRNA expression (PCR). Such identified primary human chondrocyte cells may therefore be used in transplantation techniques such as the well-documented Autologous Chondrocyte Transplantation (ACT) technique.

The results of the FACS analysis as shown in Appendix C below show that a population of cells (mesenchymal stem cells) may be identified by use of the mAb against α10 from a mixed population of human mononuclear cells (hMNCs). Appendix C shows FACS analysis identifying a population of cells (mesenchymal stem cells) from a mixed cell population of human mononuclear cells (hMNCs) that express the integrin α10β1. Cells were identified in FACS by use of a mAb against the integrin α10β1. The mAb was produced from knowledge of the sequence of the I-domain of the integrin α1β1. The cells

are present in a ratio of approx. 1:100,000, which is what is expected from a hMNC population. The mAb is also able to detect hMSCs in FACS.

Articular chondrocytes (the cells for use in transplantation) are specialized cells of mesenchymal origin found exclusively in cartilage and are the only cell type present in articular cartilage. These are the cells that produce the extracellular matrix (ECM) proteins *e.g.* aggrecan and collagen type II as well as the integrins, $\alpha 10\beta 1$, that are present on the chondrocyte cell surface. To use the integrin $\alpha 10\beta 1$ as a marker, an antibody specific for this protein is required.

Cell surface proteins have long been used as markers for transplantation and it is well documented in the literature that such cell surface markers and antibodies developed against them are used for this purpose. For example, CD34+ is an antigen expressed on the surface of early hematopoeitic stem cells and progenitors that is useful in several areas of clinical stem cell transplantation. Section of CD34+ cells for transplantation has been facilitated by development of monoclonal antibodies to the cell surface antigen.

The Office Action, on page 5, last paragraph, states that Lehnert *et al.* disclose that the $\alpha 10$ transcript is not restricted to chondrocytes and therefore it is unclear that it can be used as a marker. Applicants note difference between mRNA expression and protein expression. It is known in the art and well documented that even if a cell expresses mRNA for a protein there is no guarantee this protein will be transcribed and produced by the cells. Thus a cell may express $\alpha 10$ mRNA in twenty-four different tissues but the protein itself may only be present in one or more of these tissues. This has been documented in the

literature for vascular endothelial growth factor (VEGF) transcripts, where 3 transcripts were detected but only VEGF165 protein was expressed.

Claims 1, 23-25, 76 and 126 stand rejected under 35 U.S.C. § 112, first paragraph, as purportedly containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors had possession of the claimed invention.

Regarding fragments of α10, Applicants note that collagen binds to the I-domain of α10β1 in an ELISA assay described below. To test the functionality of the I-domains, they were coupled to biotin and added to dishes coated with collagen-type II (CII), fibronectin (FN) or albumin (BSA) (*see* Appendix D). Appendix D provides results from an ELISA assay. Binding studies demonstrating that α10 I-domain bound to collagen type II and that the binding is dependent on divalent cations (Mg^{2+}). The binding studies demonstrated that α10 I-domain bound to collagen type II and that the binding was dependent on divalent cations (Mg^{2+}). EDTA, which binds and thereby blocks the effect of divalent cations inhibited the interaction between the I-domain and collagen. Fibronectin and albumin did not promote binding of the I-domain showing that the interaction with collagen type II is specific. Taken together the binding studies demonstrated that the α10 I-domain has a function that is similar to the intact integrin α-chain.

Rejections under 35 U.S.C. § 102 and 103(a)

Claims 1, 23-24 and 126 stand rejected under 35 U.S.C. § 102(a) as purportedly anticipated by Camper *et al.* (*J. Biol. Chem.* 273(7): 20383-20389 (1998)). Camper *et al.* purportedly disclose collagen binding integrin subunit α10 comprising claimed SEQ ID NO:2, a fragment of the integrin subunit α10, wherein the fragment is a peptide comprising the amino acid sequence SEQ ID NO:7, I-domain, transmembrane domain, and short cytoplasmic domain fragments.

Claims 1 and 126 stand rejected under 35 U.S.C. § 102(b) as purportedly anticipated by U.S. Patent No. 5,686,059. The '059 patent purportedly discloses a nine amino acid sequence which bind collagen (see referenced SEQ ID NO: 34, comprising a fragment of claimed SEQ ID NQ:2 at positions, wherein the fragment is part of the I-domain. The Examiner argues that while the prior art teachings may be silent as to the "a marker or target in transplantation of cartilage or chondrocytes", the product the reference is the same as the claimed product.

Claims 1 and 126 stand rejected under 35 U.S.C. § 102(b) as purportedly anticipated by Takada *et al.* (IDS Ref No. 6). Takada *et al.* purportedly disclose a human α3 subunit and an integrin receptor for collagen. Takada *et al.* purportedly further disclose a nine amino acid sequence of metal binding domains general structure.

For proving anticipation, "anticipation requires the presence in a single prior art disclosure of all elements of a claimed invention as arranged in the claims." Jamesbury Corp. v. Litton Industrial Products, Inc. 225 U.S.P.Q. 253, 256 (Fed. Cir. 1985). The

cited reference does not describe or suggest all of the elements of the rejected claims, as discussed in greater detail below.

Claims 76 stands rejected under 35 U.S.C. § 103(a) as purportedly unpatentable over Camper *et al.,* Takada *et al.* or U.S. Patent No. 5,686,059 in view of U.S. Patent No. 5,853,987. The Examiner argues that it would have been obvious to the skilled artisan to formulate the α10 subunit, fragments and/or homologue taught by the '059, Camper *et al.* and Takada *et al.* in a composition as taught by the '987 patent.

Applicants respectfully traverse this rejection, on the grounds that the *prima facie* case of obviousness has not been established relative to the claimed invention. Rejecting a claimed invention based on its obviousness over prior art requires that the Office Action support such a rejection by establishing the invention's *prima facie* obviousness. Evaluation of whether cited references provide the necessary description requires consideration of

> (1) whether the prior art would have suggested to those of ordinary skill in the art that they should make the claimed composition or device, or carry out the claimed process; and (2) whether the prior art would also have revealed that in so making or carrying out, those of ordinary skill would have a reasonable expectation of success. *See In re* Dow Chemical Co., . . . 5 U.S.P.Q.2d 1529, 1531 (Fed. Cir. 1988). Both the suggestion and the reasonable expectation of success must be founded in the prior art, not in the applicant's disclosure.

In re Vaeck, 20 U.S.P.Q.2d 1438, 1442 (Fed. Cir. 1991). The cited references fail to meet these requirement, as discussed in detail below.

Camper

Applicants note that Camper *et al.*, (*J. biol. Chem.* 273(7):20383-20389), is the work of the inventor of the present application. The full author list if Camper L, Hellman U, Lundgren-Åkerlund E. The inventor of the present invention is the last author, *i.e.*, Lundgren-Åkerlund. The priority documents are submitted herewith.

U.S. Patent No. 5,686,059

U.S. Patent No. 5,686,059 does not recite, or even suggest, all of the elements of the claimed invention. The '059 patent discloses a nine amino acid sequence which binds to collagen, we herewith provide our comments. It discloses a protein known to be an integral part of the extracellular matrix of cartilage (Cartilage Matrix Protein CMP). In addition, a collagen-binding motif (CBS1) of 8-10 amino acids is claimed (page 3, line 31 *et seq.*). This motif has the sequence CMP1 (TDLVFIIDSS) and CMP2 (LDLVFLIDGS).

Applicants note that the sequence DIVIVLDGS and VIVLDGS were aligned in a BLAST Search (*see* Appendix E). When searching those proteins showing a 100% homology, the search showed that the sequence (DI)VIVLDGS is 100% conserved in the α subunits of the integrins $\alpha 1\beta 1$, $\alpha 10\beta 1$ and $\alpha 11\beta 1$ from different species, *i.e.*, human, rate and mouse. On performing the alignment, the sequences CMP1 (TDLVFIIDSS) and CMP2 (LDLVFLIDGS) were not found.

Applicants further note that the CBS-1 motif (SEQ ID NO:34) as recited in U.S. Patent No. 5,686,059 is the integrin $\alpha 1\beta 1$ (alternatively known as VLA-1). This is the only

sequence that gives a 100% match to DIVILDGS. Applicants further note that the α1 integrin subunit is not a homologue to α10.

As stated in U.S. Patent No. 5,686,059, the CBS-1 motif is found in a large number of other proteins and the exact amino acid sequence varies depending on the protein (SEQ no 5-36). The '059 patent states on page 3, lines 41-46, that this amino acid sequence is found in other CMP-like domains of other proteins. Applicants submit that one could equally well have decided that this *integrin-line* domain is also found in the CMP proteins (CMP1 and CMP2).

Applicants refer to Appendix E, showing sequences producing significant alignments showing a 100% homology to the sequence (DI)VIVLDGS. This sequence is 100% conserved in the α subunits of the integrins α1β1, α10β1 and α11β1 from different species, *i.e.*, human, rat and mouse.

In addition, Applicants stress that a single modification in the collagen-binding domain (I-domain) of the integrin, where the DIVILDGS is located, may lead to a change in the binding properties of the integrin, *i.e.*, in the α2 I-domain, D^{219} is important for binding to collagen type I. Mutating D to R at this position abolishes the ability of α2 to adhere to type I. This shows that because the CBS-1 motif described in the U.S. patent is not 100% identical to the integrin α10 then it is not possible to deduce any conclusions with respect as to whether it binds/does not bind, collagen in a similar manner to α10.

Takada *et al.*

Applicants submit that Takeda *et al.* is not related to the α-10 integrin subunit, neither suggests nor discloses anything that will lead the skilled artisan to the existence of this subunit. There is nothing in the cited references to lead the skilled artisanto use the new (and previously unknown) subunit α10 according to claimed methods. Takada *et al.* disclose the cloning and isolation of the α-3 subunit of human α3-β1 (=VLA3). the α-3 amino acid sequence shows 25-37% similarity (identity) to other integrin α subunits, with the highest degree of similarity to the α-6 sequence (37%) and less similarity to those α subunits that have I-domains (15-20%). The α3 subunit shows about 20% identify to the α10 subunit. The human α-3 sequence is 89% identical to hamster galactoprotein b3, and 70% similar (identical) to chicken CSAT antigen band 2 protein, suggesting that these two polypeptides are homologues of human α3.

It is well known in the art that different integrins and subunits thereof are not homologues to each other. Integrin α subunits are different proteins with different properties and functions. As they have different properties and functions, they are not interchangable, only integrin α2 β binds to collagen and furthermore comprises an I-domain. Thus, the integrin subunits α3, α4 and α6 do not bind to collagen and do not comprise an I-domain. The integrin α subunits share an overall identify of only 20-40%. Furthermore, different genes encode the integrin α subunits and the genes are located on different chromosomes.

By way of further explanation, Applicants provide a BLAST sequence comparison between the two known variants of α3 (variant a and variant b) and α10. The result of the BLAST search is shown in Appendix E. In both instances, the results show that there is no similarity between these two integrins. They bear no resemblance to each other, are not structurally related and cannot be compared in anyway.

Thus, Applicants request that these rejections be withdrawn.

CONCLUSION

In view of the foregoing, further and favorable action in the form of a Notice of Allowance is believed to be next in order. Such action is earnestly solicited.

In the event that there are any questions relating to this application, it would be appreciated if the Examiner would telephone the undersigned attorney concerning such questions so that prosecution of this application may be expedited.

In the event any further fees are due to maintain pendency of this application, the Examiner is authorized to charge such fees to Deposit Account No. 02-4800.

Respectfully submitted,

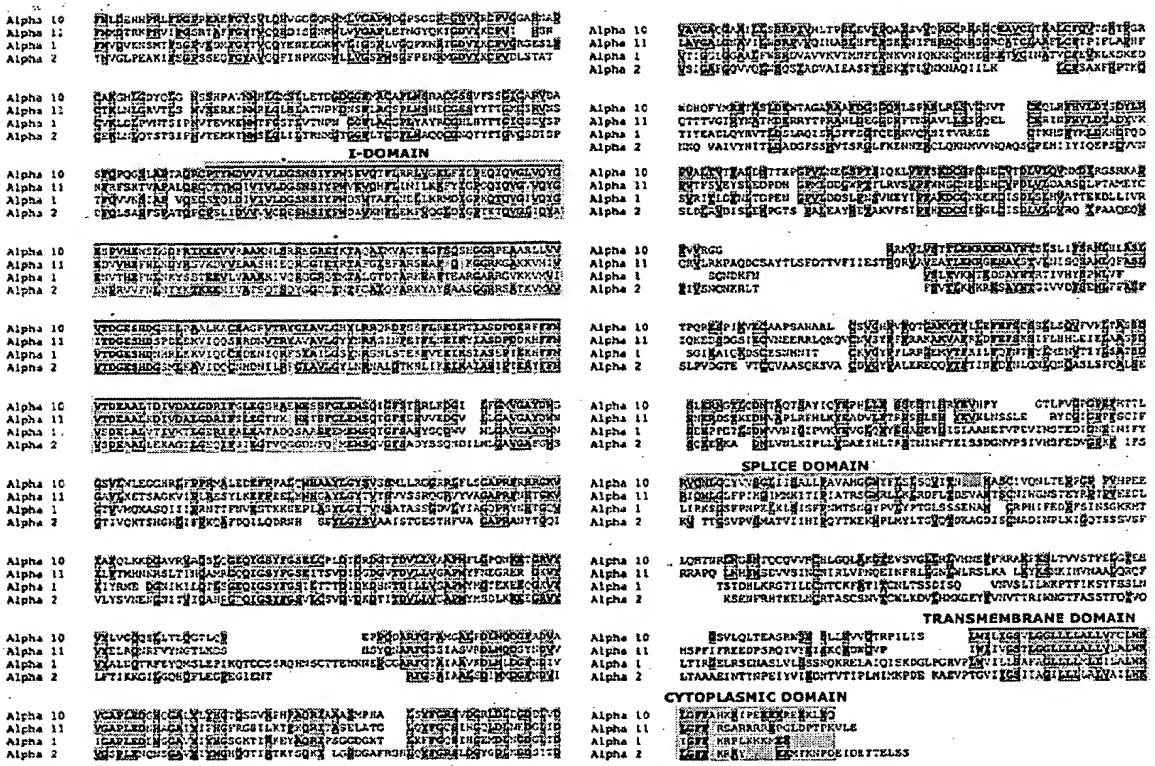
BURNS, DOANE, SWECKER & MATHIS, L.L.P.

Date: December 22, 2003

By: _____
Deborah H. Yellin
Registration No. 45,904

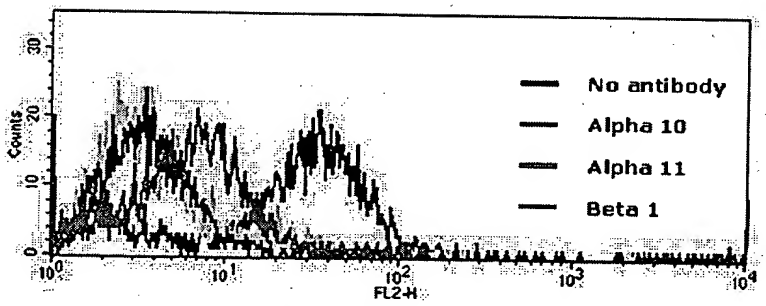
P.O. Box 1404
Alexandria, Virginia 22313-1404
(703) 836-6620

APPENDIX A



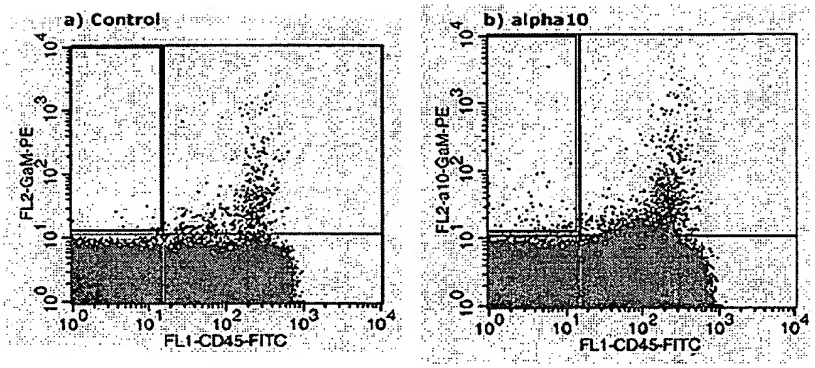
Sequence alignment of four collagen binding integrins (allpha10, alpha11, alpha1 and alpha2) – see figure 1 below. Lehnert *et al* (Cytogenet Cell Genet, 87:238-244, 1999).

APPENDIX B



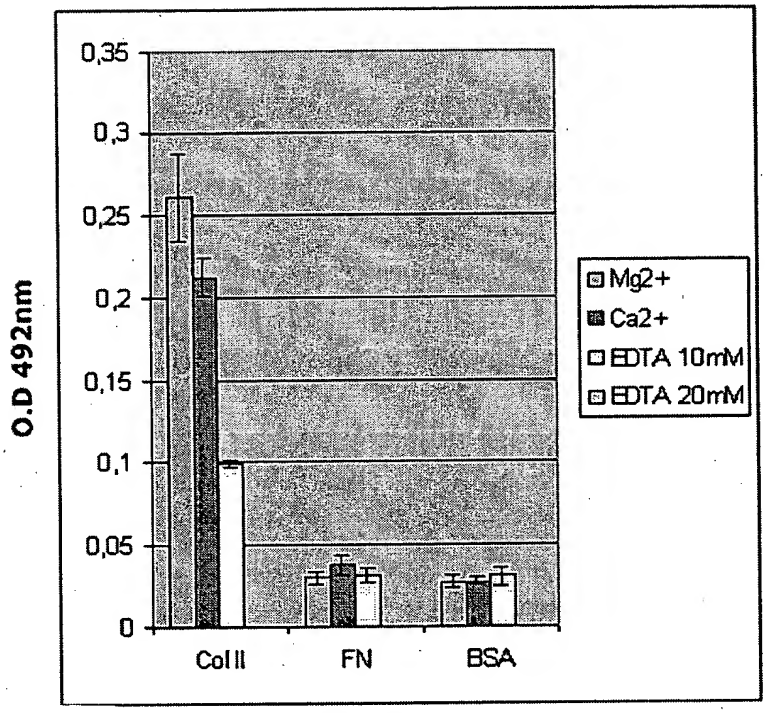
FACS analysis identifying primary human chondrocytes that express the integrin alpha10beta1. Cells were identified in FACS by use of a mAb against the integrin alpha10beta1. The mAb was produced from knowledge of the sequence of the I-domain of the integrin alpha1beta1.

APPENDIX C



FACS analysis identifying a population of cells (mesenchymal stem cells) from a mixed cell population of human mononuclear cells (hMNCs) that express the integrin alpha10beta1. Cells were identified in FACS by use of a mAb against the integrin alpha10beta1. The mAb was produced from knowledge of the sequence of the I-domain of the integrin alpha1beta1.

APPENDIX D



Results form ELISA described in text above. Binding studies demonstrating that alpha10 I-domain bound to collagen type II and that the binding is dependent on divalent cations (Mg^{2+}).

APPENDIX E

Related Structures

Sequences producing significant alignments:	Score (bits)	E Value
gi|34864154|ref|XP_236320.2| similar to a11 integrin [Rattu...	31	2.5
gi|13591884|ref|NP_112256.1| integrin alpha 1; integrin, al...	31	2.5
gi|1079413|pir||A55348 integrin alpha-1 - chicken (fragment)	31	2.5
gi|2829468|sp|P56199|ITA1_HUMAN Integrin alpha-1 (Laminin a...	31	2.5
gi|31657142|ref|NP_852478.1| integrin, alpha 1 precursor; v...	31	2.5
gi|8569519|pdb|1QC5|B Chain B, I Domain From Integrin Alpha...	31	2.5
gi|30749469|pdb|1MHP|A Chain A, Crystal Structure Of A Chim...	31	2.5
gi|32490563|ref|NP_795896.2| integrin alpha 11; integrin a1...	31	2.5
gi|7766811|pdb|1CK4|A Chain A, Crystal Structure Of Rat A1b...	31	2.5
gi|5915662|gb|AAD51919.2| integrin alpha 11 subunit precurs...	31	2.5
gi|34810098|pdb|1QCY|A Chain A, The Crystal Structure Of Th...	31	2.5
gi|2582830|dbj|BAA23160.1| alpha1 integrin [Gallus gallus]	31	2.5
gi|35193068|gb|AAH58716.1| Integrin alpha 11 [Mus musculus]	31	2.5
gi|8569518|pdb|1QC5|A Chain A, I Domain From Integrin Alpha...	31	2.5
gi|19923397|ref|NP_036343.2| integrin, alpha 11 [Homo sapie...	31	2.5
gi|3183041|sp|Q90615|ITA1_CHICK Integrin alpha-1 (Laminin a...	31	2.5

Sequences producing significant alignments showing a 100% homology to the sequence (DI)VIVLDGS. This sequence is 100% conserved in the alpha subunits of the integrins alpha1beta1, alpha10beta1 and alpha11beta1 from different species i.e. human, rat and mouse.

APPENDIX E

NCBI Blast 2 Sequences results

PubMed Entrez BLAST OMIM Taxonomy Structure

BLAST 2 SEQUENCES RESULTS VERSION BLASTN 2.2.6 [Apr-09-2003]

Match: 1 Mismatch: -2 gap open: 5 gap extension: 2

x_dropoff: 50 expect: 10.000000 wordsize: 11 Filter ☑ Align

Sequence 1	gi 4504746	Homo sapiens integrin, **alpha 3** (antigen CD49C, alpha 3 subunit of VLA-3 receptor) (ITGA3), **transcript variant a,** mRNA	**Length** 4637
Sequence 2	gi 38569397	Homo sapiens integrin, **alpha 10** (ITGA10), mRNA	**Length** 5189

No significant similarity was found

BLAST 2 SEQUENCES RESULTS VERSION BLASTN 2.2.6 [Apr-09-2003]

Match: 1 Mismatch: -2 gap open: 5 gap extension: 2

x_dropoff: 50 expect: 10.000000 wordsize: 11 Filter ☑ Align

Sequence 1	gi 6006010	Homo sapiens integrin, alpha 3 (antigen CD49C, alpha 3 subunit of VLA-3 receptor) (ITGA3), transcript **variant b**, mRNA	**Length** 4495
Sequence 2	gi 38569397	Homo sapiens integrin, alpha 10 (ITGA10), mRNA	**Length** 5189

No significant similarity was found

Figure 6 – BLAST sequence comparison of the two known variants of alpha3 (variant a and b) and alpha10. No significant similarity was found.

Please note that our client would like to use the possibility to file CIP applications of the ommitted material from the present application.

APPENDIX E

Sequence Alignment for VIVLDGS

results of BLAST

BLASTP 2.2.6 [Apr-09-2003]
Reference:
Altschul, Stephen F., Thomas L. Madden, Alejandro A. Schäffer, Jinghui Zhang, Zheng Zhang, Webb Miller, and David J. Lipman (1997), "Gapped BLAST and PSI-BLAST: a new generation of protein database search programs", Nucleic Acids Res. 25:3389-3402.

RID: 1070637397-29593-205031717772.BLASTQ3

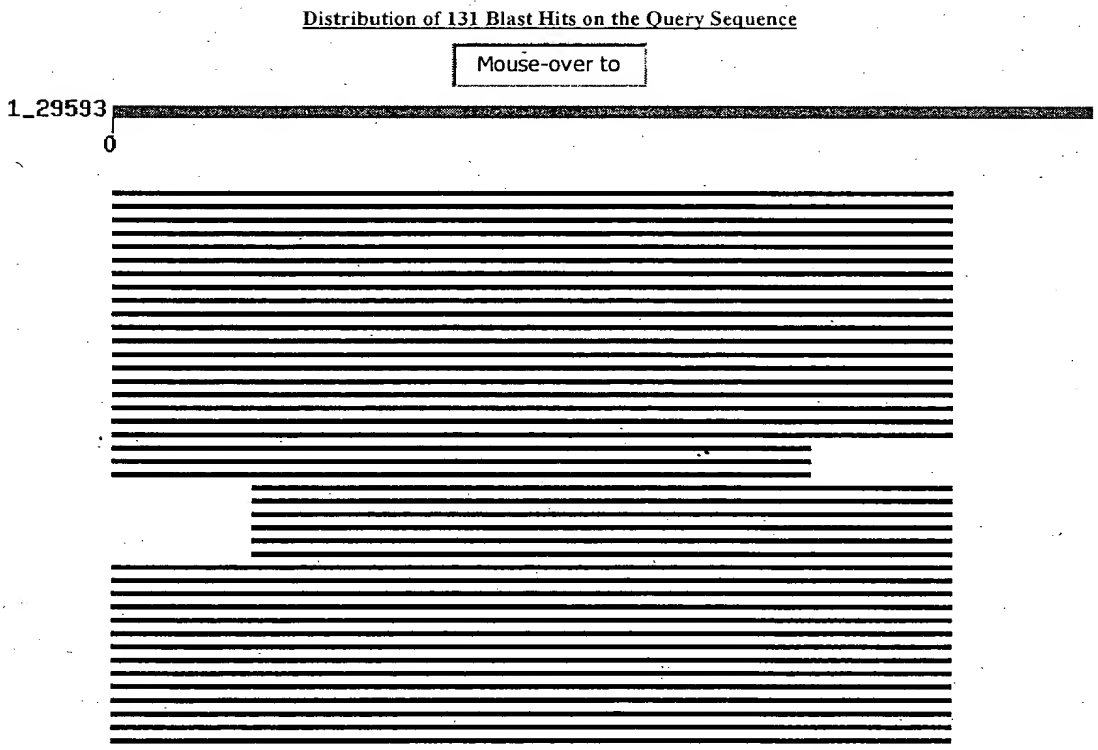
Query=
(7 letters)

Database: All non-redundant GenBank CDS translations+PDB+SwissProt+PIR+PRF
1,550,899 sequences; 506,521,537 total letters

If you have any problems or questions with the results of this search please refer to the **BLAST FAQs**

Taxonomy reports

APPENDIX E



Sequences producing significant alignments:	Score (bits)	E Value
gi|34864154|ref|XP_236320.2| similar to all integrin [Rattu...	24	50
gi|13591884|ref|NP_112256.1| integrin alpha 1; integrin, al...	24	50
gi|2829468|sp|P56199|ITA1_HUMAN Integrin alpha-1 (Laminin a...	24	50
gi|31657142|ref|NP_852478.1| integrin, alpha 1 precursor; v...	24	50
gi|8569519|pdb|1QC5|B Chain B, I Domain From Integrin Alpha...	24	50
gi|30749469|pdb|1MHP|A Chain A, Crystal Structure Of A Chim...	24	50

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gi|32490563|ref|NP_795896.2| integrin alpha 11; integrin al...	24	50
gi|7766811|pdb|1CK4|A Chain A, Crystal Structure Of Rat Alb...	24	50
gi|5915662|gb|AAD51919.2| integrin alpha 11 subunit precurs...	24	50
gi|34810098|pdb|1QCY|A Chain A, The Crystal Structure Of Th...	24	50
gi|38077326|ref|XP_207773.3| similar to integrin alpha 10 s...	24	50
gi|7385003|gb|AAF61638.1| integrin alpha 10 subunit [Homo s...	24	50
gi|38569398|ref|NP_003628.2| integrin, alpha 10 precursor [...	24	50
gi|35193068|gb|AAH58716.1| Integrin alpha 11 [Mus musculus]	24	50
gi|8569518|pdb|1QC5|A Chain A, I Domain From Integrin Alpha...	24	50
gi|19923397|ref|NP_036343.2| integrin, alpha 11 [Homo sapie...	24	50
gi|34858268|ref|XP_227469.2| similar to integrin alpha 10 s...	24	50
gi|38077635|ref|XP_112192.4| similar to integrin alpha 10 s...	24	50
gi|12643639|sp|O75578|ITAG_HUMAN Integrin alpha-10 precurso...	24	50
gi|27733291|ref|XP_224769.1| similar to transketolase [Ratt...	21	290
gi|20864314|ref|XP_134200.1| RIKEN cDNA 4933401I19 [Mus mus...	21	290
gi|12855432|dbj|BAB30335.1| unnamed protein product [Mus mu...	21	290
gi|13386276|ref|NP_082279.1| RIKEN cDNA 2310042P20 [Mus mus...	21	389
gi|6680482|ref|NP_032425.1| integrin, alpha E, epithelial-a...	21	389
gi|27370456|ref|NP_766532.1| integrin, alpha E, epithelial-...	21	389
gi|4809045|gb|AAD30063.1| Itgae protein [Mus sp.]	21	389
gi|3236344|gb|AAC23663.1| integrin alpha E2 [Rattus norvegi...	21	389
gi|25742632|ref|NP_113956.1| integrin alpha E1, epithelial-...	21	389
gi|16549223|dbj|BAB70780.1| unnamed protein product [Homo s...	21	521
gi|34328930|ref|NP_000874.2| inosine monophosphate dehydrog...	21	521
gi|34328209|ref|NP_035959.2| inosine 5'-phosphate dehydroge...	21	521
gi|106722|pir||A35566 IMP dehydrogenase (EC 1.1.1.205) I - ...	21	521
gi|25014074|sp|P20839|IMD1_HUMAN Inosine-5'-monophosphate d...	21	521
gi|37546586|ref|XP_066634.3| similar to Inosine-5-monophosp...	21	521
gi|34328928|ref|NP_899066.1| inosine monophosphate dehydrog...	21	521
gi|37546579|ref|XP_093044.2| similar to IMP dehydrogenase (...	21	521
gi|15208185|dbj|BAB63117.1| hypothetical protein [Macaca fa...	20	700
gi|3929114|gb|AAC79806.1| putative lung tumor suppressor [H...	20	700
gi|14249981|gb|AAH08377.1| EPB41L3 protein [Homo sapiens]	20	700
gi|37541979|ref|XP_353111.1| hypothetical protein XP_353110...	20	700
gi|32490572|ref|NP_036439.2| erythrocyte membrane protein b...	20	700
gi|13544009|gb|AAH06141.1| EPB41L3 protein [Homo sapiens]	20	700
gi|4589618|dbj|BAA76831.1| KIAA0987 protein [Homo sapiens]	20	700
gi|38073595|ref|XP_354685.1| similar to chromosome 14 open ...	19	1260
gi|34881880|ref|XP_346378.1| similar to transketolase-like ...	19	1690
gi|2585776|gb|AAB83983.1| multidrug resistance protein [Hom...	19	1690
gi|3928489|emb|CAA77028.1| titin [Oryctolagus cuniculus]	19	1690
gi|15620871|dbj|BAB67799.1| KIAA1906 protein [Homo sapiens]	19	1690
gi|33285008|ref|NP_689525.2| glycosyltransferase-like 1B; o...	19	1690
gi|2585774|gb|AAB83981.1| multidrug resistance protein [Hom...	19	1690
gi|6563236|gb|AAF17212.1| protein x 0001 [Homo sapiens]	19	1690
gi|11128023|ref|NP_061752.1| protocadherin gamma subfamily ...	19	1690
gi|34190015|gb|AAH25382.2| TKTL1 protein [Homo sapiens]	19	1690
gi|14589880|ref|NP_061739.2| protocadherin gamma subfamily ...	19	1690
gi|9955960|ref|NP_063957.1| ATP-binding cassette, sub-famil...	19	1690
gi|19747267|ref|NP_596869.1| titin isoform N2-A; connectin;...	19	1690
gi|7428836|pir||DVHUAR multidrug resistance protein (cell l...	19	1690
gi|7020598|dbj|BAA91193.1| unnamed protein product [Homo sa...	19	1690
gi|9955956|ref|NP_063955.1| ATP-binding cassette, sub-famil...	19	1690
gi|28892835|ref|NP_795964.1| RIKEN cDNA A330035P11 gene [Mu...	19	1690
gi|28892727|ref|NP_795900.1| RIKEN cDNA D830007G01 gene [Mu...	19	1690
gi|17433153|sp|O60245|PCH7_HUMAN Protocadherin 7 precursor ...	19	1690
gi|29893528|gb|AAN65348.1| multidrug resistance protein 1A ...	19	1690
gi|31559852|ref|NP_808566.2| expressed sequence BB049667 [M...	19	1690
gi|2585775|gb|AAB83982.1| multidrug resistance protein [Hom...	19	1690
gi|2585773|gb|AAB83980.1| multidrug resistance protein [Hom...	19	1690
gi|9955958|ref|NP_063956.1| ATP-binding cassette, sub-famil...	19	1690
gi|27369974|ref|NP_766258.1| glycosyltransferase-like 1B; g...	19	1690
gi|34856556|ref|XP_230290.2| similar to glycosyltransferase...	19	1690
gi|33621129|gb|AAQ23148.1| multidrug resistance-associated ...	19	1690
gi|22095683|sp|Q9NYQ8|FAT2_HUMAN Protocadherin Fat 2 precur...	19	1690
gi|28972313|dbj|BAC65610.1| mKIAA0609 protein [Mus musculus]	19	1690
gi|21751857|dbj|BAC04053.1| unnamed protein product [Homo s...	19	1690

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gi|33871368|gb|AAH13396.1|	TTN protein [Homo sapiens]	19	1690
gi|27479782|ref|XP_114973.3|	similar to receptor tyrosine k...	19	1690
gi|6678848|ref|NP_032602.1|	ATP-binding cassette, sub-famil...	19	1690
gi|13385584|ref|NP_080361.1|	RIKEN cDNA 3110049J23 [Mus mus...	19	1690
gi|38080787|ref|XP_144572.3|	similar to KIAA1906 protein [M...	19	1690
gi|5689557|dbj|BAA83062.1|	KIAA1110 protein [Homo sapiens]	19	1690
gi|7512300|pir||T00042	BH-protocadherin PCDH7 (clone BH-Pcd...	19	1690
gi|13787217|ref|NP_001438.1|	FAT tumor suppressor 2 precurs...	19	1690
gi|27357193|gb|AAN86532.1|	multidrug resistance-associated ...	19	1690
gi|17066106|emb|CAD12457.1|	Novex-3 Titin Isoform [Homo sap...	19	1690
gi|9955954|ref|NP_063954.1|	ATP-binding cassette, sub-famil...	19	1690
gi|9955950|ref|NP_063915.1|	ATP-binding cassette, sub-famil...	19	1690
gi|18087751|ref|NP_291061.1|	protocadherin gamma subfamily ...	19	1690
gi|14589933|ref|NP_115832.1|	protocadherin 7 isoform b prec...	19	1690
gi|18202860|sp|Q9DCG6|PHZ2_MOUSE	Probable oxidoreductase 06...	19	1690
gi|26337085|dbj|BAC32226.1|	unnamed protein product [Mus mu...	19	1690
gi|34851308|ref|XP_344726.1|	similar to acetylglucosaminylt...	19	1690
gi|26351245|dbj|BAC39259.1|	unnamed protein product [Mus mu...	19	1690
gi|34868050|ref|XP_222527.2|	ATP-binding cassette, sub-fami...	19	1690
gi|20143914|ref|NP_003310.2|	titin isoform N2-B; connectin;...	19	1690
gi|20143916|ref|NP_596870.1|	titin isoform novex-3; connect...	19	1690
gi|7452074|pir||T00256	hypothetical protein KIAA0609 - human	19	1690
gi|20143918|ref|NP_597676.1|	titin isoform novex-1; connect...	19	1690
gi|9055302|ref|NP_061234.1|	protocadherin 7; BH-protocadher...	19	1690
gi|7110727|ref|NP_036385.1|	transketolase-like 1; Transketo...	19	1690
gi|17066105|emb|CAD12456.1|	Titin [Homo sapiens]	19	1690
gi|7512299|pir||T00041	BH-protocadherin PCDH7 (clone BH-Pcd...	19	1690

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Alignments

>gi|34864154|ref|XP_236320.2| similar to all integrin [Rattus norvegicus]
Length = 1212

Score = 24.0 bits (49), Expect = 50
Identities = 7/7 (100%), Positives = 7/7 (100%)

Query: 1 VIVLDGS 7
VIVLDGS
Sbjct: 155 VIVLDGS 161

>gi|13591884|ref|NP_112256.1| integrin alpha 1; integrin, alpha 1 [Rattus norvegicus]
gi|124941|sp|P18614|ITA1_RAT Integrin alpha-1 precursor (Laminin and collagen receptor) (VLA-1)
(CD49a)
gi|111872|pir||A35854 integrin alpha-1 chain precursor - rat
gi|56494|emb|CAA36384.1| unnamed protein product [Rattus norvegicus]
Length = 1180

Score = 24.0 bits (49), Expect = 50
Identities = 7/7 (100%), Positives = 7/7 (100%)

Query: 1 VIVLDGS 7
VIVLDGS
Sbjct: 174 VIVLDGS 180

Score = 15.5 bits (29), Expect = 17758
Identities = 5/6 (83%), Positives = 5/6 (83%)

Query: 1 VIVLDG 6
VIV DG
Sbjct: 277 VIVTDG 282

>gi|2829468|sp|P56199|ITA1_HUMAN Integrin alpha-1 (Laminin and collagen receptor) (VLA-1) (CD49a)
gi|346210|pir||A45226 integrin alpha-1 chain - human (fragment)
Length = 1151

Score = 24.0 bits (49), Expect = 50
Identities = 7/7 (100%), Positives = 7/7 (100%)

Query: 1 VIVLDGS 7
VIVLDGS
Sbjct: 146 VIVLDGS 152

Score = 15.5 bits (29), Expect = 17758
Identities = 5/6 (83%), Positives = 5/6 (83%)

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Query: 1   VIVLDG 6
           VIV DG
Sbjct: 249 VIVTDG 254


>gi|31657142|ref|NP_852478.1| integrin, alpha 1 precursor; very late activation protein 1;
          laminin and collagen receptor [Homo sapiens]
          Length = 1179

 Score = 24.0 bits (49), Expect =    50
 Identities = 7/7 (100%), Positives = 7/7 (100%)

Query: 1   VIVLDGS 7
           VIVLDGS
Sbjct: 174 VIVLDGS 180



 Score = 15.5 bits (29), Expect = 17758
 Identities = 5/6 (83%), Positives = 5/6 (83%)

Query: 1   VIVLDG 6
           VIV DG
Sbjct: 277 VIVTDG 282


>gi|8569519|pdb|1QC5|B Chain B, I Domain From Integrin Alphal-Betal
          Length = 192

 Score = 24.0 bits (49), Expect =    50
 Identities = 7/7 (100%), Positives = 7/7 (100%)

Query: 1   VIVLDGS 7
           VIVLDGS
Sbjct: 7   VIVLDGS 13
```

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```
 Score = 15.5 bits (29), Expect = 17758
 Identities = 5/6 (83%), Positives = 5/6 (83%)

Query: 1   VIVLDG 6
           VIV DG
Sbjct: 110 VIVTDG 115


>gi|30749469|pdb|1MHP|A Chain A, Crystal Structure Of A Chimeric Alphal Integrin I-Domain
          In Complex With The Fab Fragment Of A Humanized
          Neutralizing Antibody
 gi|30749472|pdb|1MHP|B Chain B, Crystal Structure Of A Chimeric Alphal Integrin I-Domain
          In Complex With The Fab Fragment Of A Humanized
          Neutralizing Antibody
          Length = 192

 Score = 24.0 bits (49), Expect =    50
 Identities = 7/7 (100%), Positives = 7/7 (100%)

Query: 1  VIVLDGS 7
          VIVLDGS
Sbjct: 6  VIVLDGS 12



 Score = 15.5 bits (29), Expect = 17758
 Identities = 5/6 (83%), Positives = 5/6 (83%)

Query: 1   VIVLDG 6
           VIV DG
Sbjct: 109 VIVTDG 114
```

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>gi|32490563|ref|NP_795896.2| integrin alpha 11; integrin all [Mus musculus]
 gi|32394646|gb|AAM62130.1| all integrin [Mus musculus]
          Length = 1188

 Score = 24.0 bits (49), Expect =    50
 Identities = 7/7 (100%), Positives = 7/7 (100%)

Query: 1   VIVLDGS 7
           VIVLDGS
Sbjct: 166 VIVLDGS 172


>gi|7766811|pdb|1CK4|A Chain A, Crystal Structure Of Rat Alb1 Integrin I-Domain.
 gi|7766812|pdb|1CK4|B Chain B, Crystal Structure Of Rat Alb1 Integrin I-Domain.
          Length = 198

 Score = 24.0 bits (49), Expect =    50
 Identities = 7/7 (100%), Positives = 7/7 (100%)

Query: 1  VIVLDGS 7
          VIVLDGS
Sbjct: 8  VIVLDGS 14


 Score = 15.5 bits (29), Expect = 17758
 Identities = 5/6 (83%), Positives = 5/6 (83%)

Query: 1   VIVLDG 6
           VIV DG
Sbjct: 111 VIVTDG 116
```

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>gi|5915662|gb|AAD51919.2| integrin alpha 11 subunit precursor [Homo sapiens]
          Length = 1188

 Score = 24.0 bits (49), Expect =    50
 Identities = 7/7 (100%), Positives = 7/7 (100%)

Query: 1   VIVLDGS 7
           VIVLDGS
Sbjct: 166 VIVLDGS 172


>gi|34810098|pdb|1QCY|A Chain A, The Crystal Structure Of The I-Domain Of Human Integrin
          Alphalbeta1
          Length = 193

 Score = 24.0 bits (49), Expect =    50
 Identities = 7/7 (100%), Positives = 7/7 (100%)

Query: 1  VIVLDGS 7
           VIVLDGS
Sbjct: 6  VIVLDGS 12



 Score = 15.5 bits (29), Expect = 17758
 Identities = 5/6 (83%), Positives = 5/6 (83%)

Query: 1   VIVLDG 6
           VIV DG
Sbjct: 109 VIVTDG 114


>gi|38077326|ref|XP_207773.3| similar to integrin alpha 10 subunit [Mus musculus]
          Length = 1178

 Score = 24.0 bits (49), Expect =    50
```

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 Identities = 7/7 (100%), Positives = 7/7 (100%)

Query: 1   VIVLDGS 7
           VIVLDGS
Sbjct: 169 VIVLDGS 175


>gi|7385003|gb|AAF61638.1| integrin alpha 10 subunit [Homo sapiens]
          Length = 517

 Score = 24.0 bits (49), Expect =    50
 Identities = 7/7 (100%), Positives = 7/7 (100%)

Query: 1  VIVLDGS 7
          VIVLDGS
Sbjct: 8  VIVLDGS 14


>gi|38569398|ref|NP_003628.2| integrin, alpha 10 precursor [Homo sapiens]
 gi|6650628|gb|AAF21944.1| integrin alpha 10 subunit [Homo sapiens]
          Length = 1167

 Score = 24.0 bits (49), Expect =    50
 Identities = 7/7 (100%), Positives = 7/7 (100%)

Query: 1   VIVLDGS 7
           VIVLDGS
Sbjct: 169 VIVLDGS 175


>gi|35193068|gb|AAH58716.1| Integrin alpha 11 [Mus musculus]
          Length = 1188

 Score = 24.0 bits (49), Expect =    50
 Identities = 7/7 (100%), Positives = 7/7 (100%)

Query: 1   VIVLDGS 7
           VIVLDGS
Sbjct: 166 VIVLDGS 172
```

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```
>gi|8569518|pdb|1QC5|A Chain A, I Domain From Integrin Alphal-Betal
          Length = 192

 Score = 24.0 bits (49), Expect =    50
 Identities = 7/7 (100%), Positives = 7/7 (100%)

Query: 1  VIVLDGS 7
          VIVLDGS
Sbjct: 7  VIVLDGS 13


 Score = 15.5 bits (29), Expect = 17758
 Identities = 5/6 (83%), Positives = 5/6 (83%)

Query: 1    VIVLDG 6
          VIV DG
Sbjct: 110 VIVTDG 115


>gi|19923397|ref|NP_036343.2| integrin, alpha 11 [Homo sapiens]
 gi|12643894|sp|Q9UKX5|ITAH_HUMAN Integrin alpha-11 precursor
 gi|6013141|gb|AAF01258.1| integrin alpha-11 subunit precursor [Homo sapiens]
          Length = 1189

 Score = 24.0 bits (49), Expect =    50
 Identities = 7/7 (100%), Positives = 7/7 (100%)

Query: 1    VIVLDGS 7
          VIVLDGS
```

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Sbjct: 166 VIVLDGS 172


>gi|34858268|ref|XP_227469.2| similar to integrin alpha 10 subunit [Rattus norvegicus]
          Length = 1172

 Score = 24.0 bits (49), Expect =    50
 Identities = 7/7 (100%), Positives = 7/7 (100%)

Query: 1   VIVLDGS 7
           VIVLDGS
Sbjct: 169 VIVLDGS 175


>gi|38077635|ref|XP_112192.4| similar to integrin alpha 10 subunit [Mus musculus]
          Length = 1178

 Score = 24.0 bits (49), Expect =    50
 Identities = 7/7 (100%), Positives = 7/7 (100%)

Query: 1   VIVLDGS 7
           VIVLDGS
Sbjct: 169 VIVLDGS 175


>gi|12643639|sp|O75578|ITAG_HUMAN Integrin alpha-10 precursor
 gi|3420888|gb|AAC31952.1| integrin subunit alpha 10 precursor [Homo sapiens]
          Length = 1167

 Score = 24.0 bits (49), Expect =    50
 Identities = 7/7 (100%), Positives = 7/7 (100%)

Query: 1   VIVLDGS 7
           VIVLDGS
Sbjct: 169 VIVLDGS 175
```

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>gi|27733291|ref|XP_224769.1| similar to transketolase [Rattus norvegicus]
          Length = 627

 Score = 21.4 bits (43), Expect =   290
 Identities = 6/6 (100%), Positives = 6/6 (100%)

Query: 1   VIVLDG 6
           VIVLDG
Sbjct: 340 VIVLDG 345


>gi|20864314|ref|XP_134200.1| RIKEN cDNA 4933401I19 [Mus musculus]
          Length = 627

 Score = 21.4 bits (43), Expect =   290
 Identities = 6/6 (100%), Positives = 6/6 (100%)

Query: 1   VIVLDG 6
           VIVLDG
Sbjct: 340 VIVLDG 345


>gi|12855432|dbj|BAB30335.1| unnamed protein product [Mus musculus]
          Length = 627

 Score = 21.4 bits (43), Expect =   290
 Identities = 6/6 (100%), Positives = 6/6 (100%)

Query: 1   VIVLDG 6
           VIVLDG
Sbjct: 340 VIVLDG 345
```

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>gi|13386276|ref|NP_082279.1| RIKEN cDNA 2310042P20 [Mus musculus]
gi|12844762|dbj|BAB26489.1| unnamed protein product [Mus musculus]
gi|13278498|gb|AAH04046.1| RIKEN cDNA 2310042P20 [Mus musculus]
Length = 660

Score = 21.0 bits (42), Expect = 389
Identities = 6/6 (100%), Positives = 6/6 (100%)

Query: 2 IVLDGS 7
IVLDGS
Sbjct: 345 IVLDGS 350

>gi|6680482|ref|NP_032425.1| integrin, alpha E, epithelial-associated [Mus musculus]
gi|2497428|sp|Q60677|ITAE_MOUSE Integrin alpha-E precursor (Integrin alpha M290)
gi|535477|gb|AAC52142.1| alpha M290 integrin
Length = 1167

Score = 21.0 bits (42), Expect = 389
Identities = 6/6 (100%), Positives = 6/6 (100%)

Query: 2 IVLDGS 7
IVLDGS
Sbjct: 198 IVLDGS 203

>gi|27370456|ref|NP_766532.1| integrin, alpha E, epithelial-associated [Mus musculus]
gi|26334103|dbj|BAC30769.1| unnamed protein product [Mus musculus]
Length = 1038

Score = 21.0 bits (42), Expect = 389
Identities = 6/6 (100%), Positives = 6/6 (100%)

Query: 2 IVLDGS 7
IVLDGS
Sbjct: 198 IVLDGS 203

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```
>gi|4809045|gb|AAD30063.1| Itgae protein [Mus sp.]
          Length = 895

 Score = 21.0 bits (42), Expect =   389
 Identities = 6/6 (100%), Positives = 6/6 (100%)

Query: 2   IVLDGS 7
           IVLDGS
Sbjct: 185 IVLDGS 190


>gi|3236344|gb|AAC23663.1| integrin alpha E2 [Rattus norvegicus]
          Length = 1167

 Score = 21.0 bits (42), Expect =   389
 Identities = 6/6 (100%), Positives = 6/6 (100%)

Query: 2   IVLDGS 7
           IVLDGS
Sbjct: 198 IVLDGS 203


>gi|25742632|ref|NP_113956.1| integrin alpha E1, epithelial-associated [Rattus norvegicus]
 gi|3236342|gb|AAC23662.1| integrin alpha E1 [Rattus norvegicus]
          Length = 1167

 Score = 21.0 bits (42), Expect =   389
 Identities = 6/6 (100%), Positives = 6/6 (100%)

Query: 2   IVLDGS 7
           IVLDGS
Sbjct: 198 IVLDGS 203
```

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>gi|16549223|dbj|BAB70780.1| unnamed protein product [Homo sapiens]
          Length = 489

 Score = 20.6 bits (41), Expect =   521
 Identities = 6/7 (85%), Positives = 6/7 (85%)

Query: 1   VIVLDGS 7
           VIVLD S
Sbjct: 245 VIVLDSS 251


>gi|34328930|ref|NP_000874.2| inosine monophosphate dehydrogenase 1 isoform a; sWSS2608 [Homo
           sapiens]
          Length = 599

 Score = 20.6 bits (41), Expect =   521
 Identities = 6/7 (85%), Positives = 6/7 (85%)

Query: 1   VIVLDGS 7
           VIVLD S
Sbjct: 355 VIVLDSS 361


>gi|34328209|ref|NP_035959.2| inosine 5'-phosphate dehydrogenase 1 [Mus musculus]=
 gi|31418432|gb|AAH53416.1| Inosine 5'-phosphate dehydrogenase 1 [Mus musculus]
          Length = 514

 Score = 20.6 bits (41), Expect =   521
 Identities = 6/7 (85%), Positives = 6/7 (85%)

Query: 1   VIVLDGS 7
           VIVLD S
Sbjct: 270 VIVLDSS 276
```

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>gi|106722|pir||A35566 IMP dehydrogenase (EC 1.1.1.205) I - human
 gi|33357127|pdb|1JCN|A Chain A, Binary Complex Of Human Type-I Inosine Monophosphate
           Dehydrogenase With 6-Cl-Imp
 gi|33357128|pdb|1JCN|B Chain B, Binary Complex Of Human Type-I Inosine Monophosphate
           Dehydrogenase With 6-Cl-Imp
          Length = 514

 Score = 20.6 bits (41), Expect =   521
 Identities = 6/7 (85%), Positives = 6/7 (85%)

Query: 1   VIVLDGS 7
           VIVLD S
Sbjct: 270 VIVLDSS 276


>gi|25014074|sp|P20839|IMD1_HUMAN Inosine-5'-monophosphate dehydrogenase 1 (IMP dehydrogenase
1)
           (IMPDH-I) (IMPD 1)
 gi|21706907|gb|AAH33622.1| IMPDH1 protein [Homo sapiens]
          Length = 514

 Score = 20.6 bits (41), Expect =   521
 Identities = 6/7 (85%), Positives = 6/7 (85%)

Query: 1   VIVLDGS 7
           VIVLD S
Sbjct: 270 VIVLDSS 276


>gi|37546586|ref|XP_066634.3| similar to Inosine-5-monophosphate dehydrogenase 1 (IMP
           dehydrogenase 1) (IMPDH-I) (IMPD 1) [Homo sapiens]
          Length = 460

 Score = 20.6 bits (41), Expect =   521
 Identities = 6/7 (85%), Positives = 6/7 (85%)
```

APPENDIX E

```
Query: 1   VIVLDGS 7
           VIVLD S
Sbjct: 221 VIVLDSS 227
```

>gi|34328928|ref|NP_899066.1| inosine monophosphate dehydrogenase 1 isoform b; sWSS2608 [Homo sapiens]
Length = 563

Score = 20.6 bits (41), Expect = 521
Identities = 6/7 (85%), Positives = 6/7 (85%)

```
Query: 1   VIVLDGS 7
           VIVLD S
Sbjct: 319 VIVLDSS 325
```

>gi|37546579|ref|XP_093044.2| similar to IMP dehydrogenase (EC 1.1.1.205) I - human [Homo sapiens]
Length = 514

Score = 20.6 bits (41), Expect = 521
Identities = 6/7 (85%), Positives = 6/7 (85%)

```
Query: 1   VIVLDGS 7
           VIVLD S
Sbjct: 270 VIVLDSS 276
```

>gi|15208185|dbj|BAB63117.1| hypothetical protein [Macaca fascicularis]
Length = 611

Score = 20.2 bits (40), Expect = 700
Identities = 6/7 (85%), Positives = 7/7 (100%)

```
Query: 1   VIVLDGS 7
           VI+LDGS
Sbjct: 118 VILLDGS 124
```

APPENDIX E

```
>gi|3929114|gb|AAC79806.1| putative lung tumor suppressor [Homo sapiens]
          Length = 503

 Score = 20.2 bits (40), Expect =   700
 Identities = 6/7 (85%), Positives = 7/7 (100%)

Query: 1  VIVLDGS 7
          VI+LDGS
Sbjct: 5  VILLDGS 11


>gi|14249981|gb|AAH08377.1| EPB41L3 protein [Homo sapiens]
          Length = 121

 Score = 20.2 bits (40), Expect =   700
 Identities = 6/7 (85%), Positives = 7/7 (100%)

Query: 1  VIVLDGS 7
          VI+LDGS
Sbjct: 5  VILLDGS 11


>gi|37541979|ref|XP_353111.1| hypothetical protein XP_353110 [Homo sapiens]
          Length = 97

 Score = 20.2 bits (40), Expect =   700
 Identities = 6/7 (85%), Positives = 7/7 (100%)

Query: 1  VIVLDGS 7
          VI+LDGS
Sbjct: 87 VILLDGS 93
```

APPENDIX E

```
>gi|32490572|ref|NP_036439.2| erythrocyte membrane protein band 4.1-like 3; differentially
          expressed in adenocarcinoma of the lung [Homo sapiens]
 gi|17433099|sp|Q9Y2J2|E4L3_HUMAN Band 4.1-like protein 3 (4.1B) (Differentially expressed in
          adenocarcinoma of the lung protein 1) (DAL-1)
         Length = 1087

 Score = 20.2 bits (40), Expect =   700
 Identities = 6/7 (85%), Positives = 7/7 (100%)

Query: 1   VIVLDGS 7
           VI+LDGS
Sbjct: 114 VILLDGS 120


>gi|13544009|gb|AAH06141.1| EPB41L3 protein [Homo sapiens]
         Length = 865

 Score = 20.2 bits (40), Expect =   700
 Identities = 6/7 (85%), Positives = 7/7 (100%)

Query: 1   VIVLDGS 7
           VI+LDGS
Sbjct: 114 VILLDGS 120


>gi|4589618|dbj|BAA76831.1| KIAA0987 protein [Homo sapiens]
         Length = 1115

 Score = 20.2 bits (40), Expect =   700
 Identities = 6/7 (85%), Positives = 7/7 (100%)

Query: 1   VIVLDGS 7
           VI+LDGS
Sbjct: 142 VILLDGS 148
```

APPENDIX E

```
>gi|38073595|ref|XP_354685.1| similar to chromosome 14 open reading frame 145 [Mus musculus]
          Length = 320

 Score = 19.3 bits (38), Expect =  1260
 Identities = 5/6 (83%), Positives = 6/6 (100%)

Query: 1   VIVLDG 6
           VI+LDG
Sbjct: 281 VIILDG 286


>gi|34881880|ref|XP_346378.1| similar to transketolase-like 1 [Rattus norvegicus]
          Length = 611

 Score = 18.9 bits (37), Expect =  1690
 Identities = 5/5 (100%), Positives = 5/5 (100%)

Query: 1   VIVLD 5
           VIVLD
Sbjct: 309 VIVLD 313


>gi|2585776|gb|AAB83983.1| multidrug resistance protein [Homo sapiens]
          Length = 1450

 Score = 18.9 bits (37), Expect =  1690
 Identities = 5/5 (100%), Positives = 5/5 (100%)

Query: 1    VIVLD 5
           VIVLD
Sbjct: 1416 VIVLD 1420
```

APPENDIX E

>gi|3928489|emb|CAA77028.1| titin (Oryctolagus cuniculus)
Length = 2000

Score = 18.9 bits (37), Expect = 1690
Identities = 5/7 (71%), Positives = 7/7 (100%)

Query: 1 VIVLDGS 7
V+VL+GS
Sbjct: 15 VVVLEGS 21

>gi|15620871|dbj|BAB67799.1| KIAA1906 protein (Homo sapiens)
Length = 593

Score = 18.9 bits (37), Expect = 1690
Identities = 5/5 (100%), Positives = 5/5 (100%)

Query: 1 VIVLD 5
VIVLD
Sbjct: 163 VIVLD 167

>gi|33285008|ref|NP_689525.2| glycosyltransferase-like 1B; ortholog of mouse
glycosyltransferase-like 1B (Homo sapiens)
gi|21755403|dbj|BAC04675.1| unnamed protein product (Homo sapiens)
Length = 721

Score = 18.9 bits (37), Expect = 1690
Identities = 5/5 (100%), Positives = 5/5 (100%)

Query: 1 VIVLD 5
VIVLD
Sbjct: 197 VIVLD 201

APPENDIX E

```
>gi|2585774|gb|AAB83981.1| multidrug resistance protein [Homo sapiens]
          Length = 1456

 Score = 18.9 bits (37), Expect =  1690
 Identities = 5/5 (100%), Positives = 5/5 (100%)

Query: 1    VIVLD 5
             VIVLD
Sbjct: 1422 VIVLD 1426



  Database: All non-redundant GenBank CDS
  translations+PDB+SwissProt+PIR+PRF
    Posted date:  Dec 4, 2003  7:45 PM
  Number of letters in database: 506,521,537
  Number of sequences in database:  1,550,899

Lambda     K      H
   0.338    0.297     1.56

Gapped
Lambda     K      H
   0.294    0.110    0.610


Matrix: PAM30
Gap Penalties: Existence: 9, Extension: 1
Number of Hits to DB: 579,563
Number of Sequences: 1550899
Number of extensions: 3825
Number of successful extensions: 911
Number of sequences better than 20000.0: 825
Number of HSP's better than 20000.0 without gapping: 825
Number of HSP's successfully gapped in prelim test: 0
Number of HSP's that attempted gapping in prelim test: 0



Number of HSP's gapped (non-prelim): 911
length of query: 7
length of database: 90,480,471
effective HSP length: 0
effective length of query: 9
effective length of database: 90,480,471
effective search space: 814324239
effective search space used: 814324239
T: 11
A: 40
X1: 15 ( 7.3 bits)
X2: 35 (14.8 bits)
X3: 58 (24.6 bits)
S1: 29 (15.9 bits)
S2: 29 (15.5 bits)
```

ATTACHMENT

OXFORD DICTIONARY OF BIOCHEMISTRY AND MOLECULAR BIOLOGY

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ATTACHMENT

homogenesis the production of offspring having the same characteristics in successive generations. *Compare* **heterogenesis**.

homogenetic describing chromosome pairing during meiosis when the pairing partners are derived from one of the original ancestors. *Compare* **heterogenetic**.

homogenic *or* **congenic** 1 describing a gamete that contains only one allele of a particular gene. 2 describing two genetic elements that are descended from a common ancestor by a known sequence of steps. 3 *an alternative word for* **homogeneous**. *Compare* **heterogenic**.

homogenize *or* **homogenise** produce a **homogenate**. —**homogenization** *or* **homogenisation** *n.*

homogenizer *or* **homogeniser** any apparatus for producing a **homogenate**.

homogenous 1 of, pertaining to, or exhibiting **homogeny**. 2 *an alternative word for* **homogeneous**.

homogentisate *or (formerly)* **alcapton** 2,5-dihydroxyphenylacetate; an intermediate in the catabolism of tyrosine and in the biosynthesis of plastoquinone and tocopherol. It is excreted in abnormally large quantities in the urine in **alcaptonuria**. *See also* **homogentisate 1,2-dioxygenase**.

homogentisate 1,2-dioxygenase EC 1.13.11.5; *systematic name*: homogentisate:oxygen 1,2-oxidoreductase (decyclizing); *other names*: homogentisicase; homogentisate oxygenase; homogentisic acid oxidase. An enzyme that catalyses the oxidation by dioxygen of homogentisate to 4-maleylacetoacetate; iron(II) is a cofactor. In the catabolism of L-tyrosine, **homogentisate** is formed from 4-hydroxyphenylpyruvate; maleylacetoacetate is converted to fumarylacetoacetate, which is split to fumarate and acetoacetate.

homogeny *(in biology)* similarity in the structure of organisms or parts of organisms because of common ancestry.

homoglycan *or* **homopolysaccharide** any polysaccharide (i.e. glycan) that contains residues of only one kind of monosaccharide (i.e. glycose) molecule. *Compare* **heteroglycan**.

homograft *an old term for* **allograft**. *Compare* **heterograft**.

homoio+ *a variant form of* **homeo+**.

homoiosmotic describing organisms with a constant internal osmotic pressure. *Compare* **poikilosmotic**.

homoiothermic *or* **homoiothermal** *or (esp. US)* **homeothermic** *or* **homeothermal** describing an organism (**poikilotherm**) that sustains a relatively constant body temperature, usually higher than that of its surroundings. *Compare* **poikilothermic**. —**homoiothermy** *or (esp. US)* **homeothermy** *n.*

homokaryon *or* **homocaryon** any cell with more than one nucleus, and in which the nuclei are all of the same genetic constitution; a tissue composed of such cells. *Compare* **heterokaryon**. —**homokaryotic** *or* **homocaryotic** *adj.*

homokaryosis *or* **homocaryosis** the condition of having a **homokaryon** or homokaryons. *Compare* **heterokaryosis**.

homolactic fermentation a type of fermentation of glucose to lactate via the **Embden–Meyerhof pathway**. *Compare* **heterolactic fermentation**.

homolog *(sometimes) the US spelling of* **homologue**.

homologous 1 having a related or similar position, structure, etc.; corresponding; exhibiting **homology**. 2 *(in chemistry)* describing compounds that form a series with successive constant differences in composition. 3 *(in biology)* of common ancestry; especially of organs and tissues that have a similar anatomical position and structure in different species by virtue of their common evolutionary origin, even though their functions may have come to differ; e.g. the wing of a bird and the forelimb of a reptile. *Compare* **analogous**. 4 *(in genetics)* describing chromosomes that pair during meiosis, each member of a homologous pair being a duplicate of one of the chromosomes contributed at syngamy by the mother or the father. 5 *(in biochemistry)* a (of sequences of residues in encoded macromolecules) having the same or similar residues at corresponding positions (*see also* **conserved**). With respect to proteins the term is used to imply a common evolutionary origin. Specifically this requires evidence based on gene structure and not merely a similarity of protein structure. b (of proteins from different species) having identical or similar functions. *Compare* **heterologous**. —**homology** *n.*

homologous antibody the antibody elicited by a specified antigen.

homologous antigen the antigen that has elicited a specified antibody.

homologous desensitization *see* **desensitization**.

homologue *or (sometimes) US* **homolog** 1 (something) exhibiting homology. 2 *(in chemistry)* any member of a **homologous** (def. 2) series of compounds. 3 *(in biology)* any one of a series of **homologous** (def. 3) organs or structures. 4 *(in genetics)* a either members of a pair of **homologous** (def. 4) chromosomes. b either one of two genes in corresponding loci in homologous chromosomes.

homology domain any of the regions in an immunoglobulin involved in forming the **immunoglobulin fold**.

homolysis *(in chemistry)* the cleavage of a covalent bond in such a manner that each of the fragments between which the bond is broken retains one of the bonding electrons; e.g. A–B → A· + B·. —**homolytic** *adj.*

homooligomer any **oligomer** made up of only one kind of constitutional repeating unit. —**homooligomeric** *adj.*

homophilic binding *(of adhesion molecules)* binding of an adhesion molecule in one cell to an identical molecule in an adjacent cell. *Compare* **heterophilic binding**.

homopolymer any polymer made up of only one kind of constitutional repeating unit. For example, cellulose contains only glucose as the monomeric unit. —**homopolymeric** *adj.*

homopolymer tailing *a jargon term for* a procedure useful in joining two types of duplex DNA molecules to form mixed dimeric circular DNA. In this procedure, homopolymer sequences of one type, e.g. poly(dA), are added to the 3′-ends of one of the populations of DNA molecules, while complementary homopolymer sequences, e.g. poly(dT), are added to the 3′-ends of the other population of DNA molecules. The two types of molecules are then annealed to form mixed dimeric circles.

homopolysaccharide *an alternative name for* **homoglycan**.

homoserine *symbol*: Hse; α-amino-γ-hydroxybutyric acid; an intermediate in the biosynthesis of cystathionine, threonine, and methionine. It also occurs in bacterial peptidoglycans and, as its *O*-guanidino derivative, in canavanine. The term normally implies the L enantiomer.

homoserine deaminase *see* **cystathionine γ-lyase**.

homoserine dehydratase *see* **cystathionine γ-lyase**.

homoserine dehydrogenase EC 1.1.1.3; *systematic name*: L-homoserine:NAD(P)$^+$ oxidoreductase; an enzyme of the pathways for the biosynthesis of methionine and threonine. It catalyses the formation of L-homoserine and NAD(P)$^+$ from L-aspartate 4-semialdehyde and NAD(P)H. Example, a homotetrameric bifunctional enzyme from *Escherichia coli*: database code AK1H_ECOLI, 820 amino acids (89.02 kDa). Amino acids 1–249 form the aspartokinase I domain, amino acids 250–470 form a large 'interface', and 471–820 form homoserine dehydrogenase; regulation is by L-Thr. Another example is from *Corynebacterium glutamicum* and *Brevibacterium lactofermentum*: database code DHOM_CORGL, 445 amino acids (46.39 kDa). *See also* **aspartokinase/homoserine dehydrogenase**.

homoserine lactone *symbol*: Hsl; α-amino-γ-butyrolactone; a substance formed by the cleavage of methionine-containing peptides by cyanogen bromide.

homosterism *or* **homostery** the phenomenon in which a second molecule of normal substrate, or a structurally similar compound, combines at the catalytic site of an enzyme leading to a modification in the reaction of the bound intermediate. *Compare* **allosterism**. —**homosteric** *adj.*

homostery *an alternative term for* **homosterism**.

homothallic describing species, e.g. of certain fungi and algae, in which a sexual spore can result from the fusion of nuclei that are genetically distinct (i.e. not necessarily homozygous), but are derived from the same thallus; thus the species is self-fertile.